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Hemodynamic monitoring in critically ill patients in paediatric ICU

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ABSTRACT

Objectives: Monitoring hemodynamics in septic shock is very challenging issue in all septic patients in pediatric intensive care units and to choose the most appropriate vasoactive drug. Aim of our study was to monitor hemodynamics and compare the effects of dopamine, nor-epinephrine and epinephrine. *Methods*: Sixty patients were divided into three groups according to vasoactive drug used either dopamine, adrenaline or noradrenaline and subjected to measure cardiac functions by echocardiography. *Results*: Adrenaline was the most powerful drug affecting cardiac function and improving cardiac index (CI) on the other side noradrenaline was the most potent affecting blood pressure. *Conclusion*: The use of echocardiography can help to choose and escalating vasoactive drug in septic shock.

Keywords: hemodynamics, septic shock, vaosactive drug, dopamine, epinephrine, nor-epinephrine, echocardiography, cardiac index

1. INTRODUCTION

Sepsis was known as life-threatening system disruption induced by a disorganized response to infection and "septic shock" the subtype of sepsis with dysfunction at circulatory and cellular/metabolic levels associated with a more risk of deaths (Singer et al., 2016). Sepsis is a major public health concern. The reported incidence of sepsis is increasing likely reflecting more co morbidities, greater recognition (Rhee et al., 2014). Despite the true number of sepsis cases isn't fully known, sepsis could be considered one of leading causes of mortality and morbidity all over the world (Fleischmann et al., 2016). Early recognition and early institution of resuscitative measures as antibiotic therapy, fluid therapy and vasoactive medications have the better effect on patient hospital course and outcome. With decreasing mortality in children, furthermore may prevent the child from entering end stages of shock (Fleischmann et al., 2016).

All previous studies recommend to start vasoactive medication after 40–60 mL/kg of fluid resuscitation if the patient still have abnormal perfusion, developed fluid overload (Lamontagne et al., 2018). In pediatrics, selection of the appropriate vasoactive agent should be driven by the clinical features of a

patient's presentation with either cold shock which is defined as low cardiac output and high systemic vascular resistance state or warm shock which is the opposite and defined as high cardiac output and low systemic vascular resistance. Dopamine and epinephrine should be used to improve cardiac output in "cold shock," whereas norepinephrine should be preferentially used to increase SVR in patients with warm shock (Martin & Weiss, 2015).

Echocardiography is a rapid, noninvasive, integrated cardiac assessment tool for patients presenting with abnormal hemodynamic state. Sepsis-induced myocardial dysfunction can be diagnosed, and responses to therapy can be monitored with echocardiography (Griffee et al., 2010). We aimed to evaluate to septic patients by echocardiography and to compare the effect of the most popular vasoctive drugs dopamine, arenaline and noradrenaline.

2. METHODS

This prospective observational study included 60 patients (male& female) with septic shock presented to Pediatric Intensive Care Unit, Children's hospital, Ain Shams University who recruited randomly from March 2019 to March 2020 after fulfilling inclusion criteria.

Inclusion and exclusion criteria

The inclusion criteria of these patients included: Patients within paediatric age group at time of enrolment aged between 30 days and 18 years. Patient presented with sepsis according to pSOFA score system at time of enrolment

Exclusion criteria included: Any structural heart disease either congenital or acquired, macrophage activation syndrome, chronic kidney disease, known Raynaud's phenomenon, after gastrointestinal surgery or having inflammatory bowel disease or other chronic disease affecting gastro intestinal tract.

Samples

The sample sizes calculate by PASS program, type-1 error (α) / 5%, power (1-β) at 90%. Based on a previous study (Backer et al., 2010), the needed sample was 60 cases.

Study procedures

Study population included Sixty Paediatric Patients admitted to Paediatric Intensive Care Unit (PICU) Ain Shams University Hospitals fulfilling criteria of septic shock. Those patients were divided randomly into three groups (group A, B, C) according to the vasoactive agent used.

Group (A): Twenty patients had septic shock had started dopamine infusion at dose ranging between 5-20 mic/kg/min The dose titrated at increases of 1μg/kg/min to achieve and maintain goal directed therapy.

Group (B): Twenty patients had septic shock had started noradrenaline infusion at dose ranging between 0.05-2 mic/kg/min. The dose titrated at increases of 0.1μg/kg/min to achieve and maintain goal directed therapy.

Group (c): Twenty patients had septic shock had started adrenaline infusion at dose ranging between 0.05-2 mic/kg/min. The dose will be titrated at increases of 0.1μg/kg/min to achieve and maintain goal directed therapy.

Titration of dose or combination therapy had been done if failed to achieve goal directed therapy.

The following was done for all patients fulfilling the inclusion criteria include detailed history, physical examination, laboratory investigations, recording of blood pressure, pulse, peripheral Temperature Urine output, central venous pressure (CVP) and pSOFA score. Echocardiography to measure ejection fraction, fraction shortening, stroke volume and cardiac index at initiation and at the termination of 24 hour after starting vaso active drug

Statistical analysis

Data analyzed using IBM© SPSS© Statistics version 22 (IBM© Corp., Armonk, NY). Median and Interquartile range for quantitative non-parametric data. Qualitative data, Frequency and percentage used. Student T-Test or Mann Whitney test used for quantitative data while chi-square test and Fisher exact test used for qualitative data. $P < 0.05$ is considered statistically significant.

3. RESULTS

Patient Data

No significant difference among patients groups who received either dopamine, noradrenaline or adrenaline regarding to age, weight, height and gender was found in the study (Table 1).

Table 1 Demographic data of studied groups

Character	Dopamine group (n=20)	Noradrenaline group (n = 20)(%)	Adrenaline group (n =38)(%)	P-value	Sig
Age (months) Median (IQR)	27.5 (6-48)	21 (9.5-48)	11 (8-42)	0.721	NS
Weight Median (IQR)	8.8 (5.4-14)	10.5 (8-13.5)	8.6 (7.4-11)	0.310	NS
Height Median (IQR)	75.5(60-98.5)	82(69-96.5)	71.5(65.5-89.5)	0.549	NS
Body surface area Median (IQR)	0-4(0.3-0.6)	0.5 (0.4-0.6)	0-4(0.4-0.5)	0.393	NS
Sex: Male Female	8 (40) 12(60)	10 (50) 10 (50)	11 (55) 9 (45)	0.627	NS

Age (month), Weight (kg), Height (cm), Body surface area (m2) Data presented as median ± IQ,

Vital data

There was a statistically significant difference in mean blood pressure between three groups as shown in (Table 2) and (figure 1, 2, 3, 4).

Table 2 A comparisons between the three studied groups regarding the vital data

Vital Data	Dopamine group (n=20)	Noradrenaline group (n = 20)(%)	Adrenaline group (n =38)(%)	P-value	Sig
HR Mean (confidence interval)	135.1 (132.3-137.9)	137.8 (135.2-140.3)	139.3 (136.7-142)	0.116	NS
MAP Mean (confidence interval)	63.74 61.85 - 65.63)	69.36 (67.37 - 71.43)	67.66 (65.8 - 69.71)	0.000**	S
CVP Mean (confidence interval)	7.54 (6.88 - 8.2)	8.39 (7.78 – 9.01)	8.65 (8.02-9.23)	0.066*	NS
Temp Mean (confidence interval)	36.91 (36.76-37.04)	36.96 (36.83-37.10)	36.79 (36.66-36.93)	0.205	NS
UOP Mean (confidence interval)	3.84 (3.12 – 3.84)	3.50 (3.17 – 3.84)	3.06 (3.72 – 3.40)	0.129	NS

MBP: mean blood pressure (mmHg), *HR:* heart rate (beat/min), *CVP:* central venous pressure (mmhg), urine output: (cc/kg/hr)

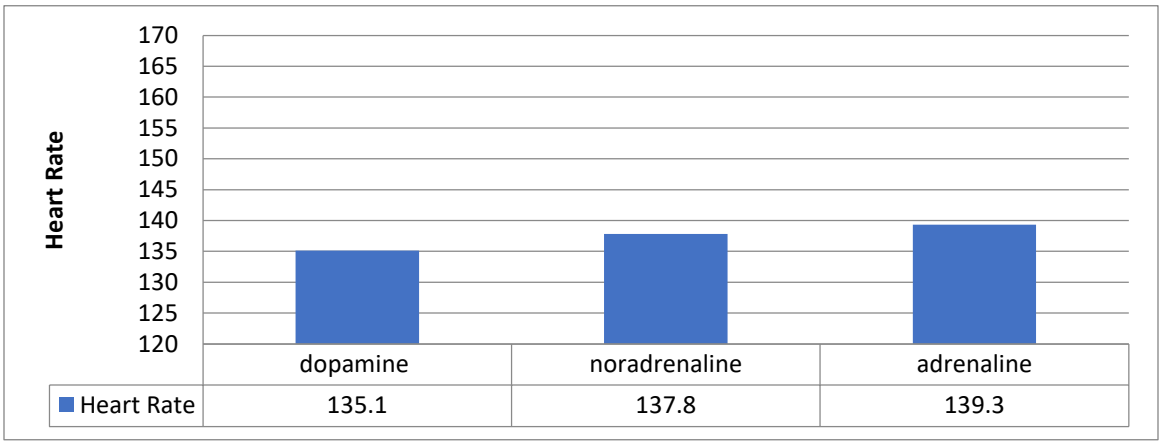

Figure 1 Heart rate in the three study groups.

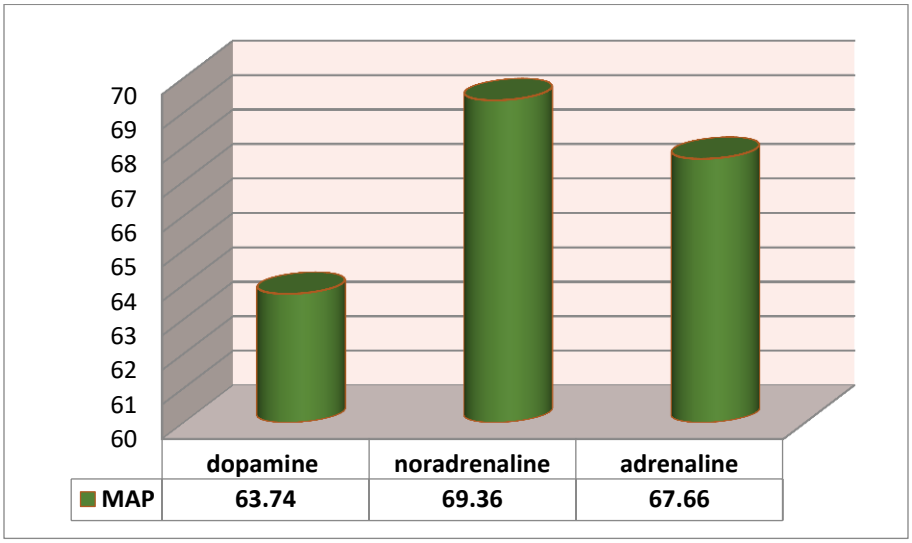

Figure 2 Mean arterial pressure (MAP) in the three study groups.

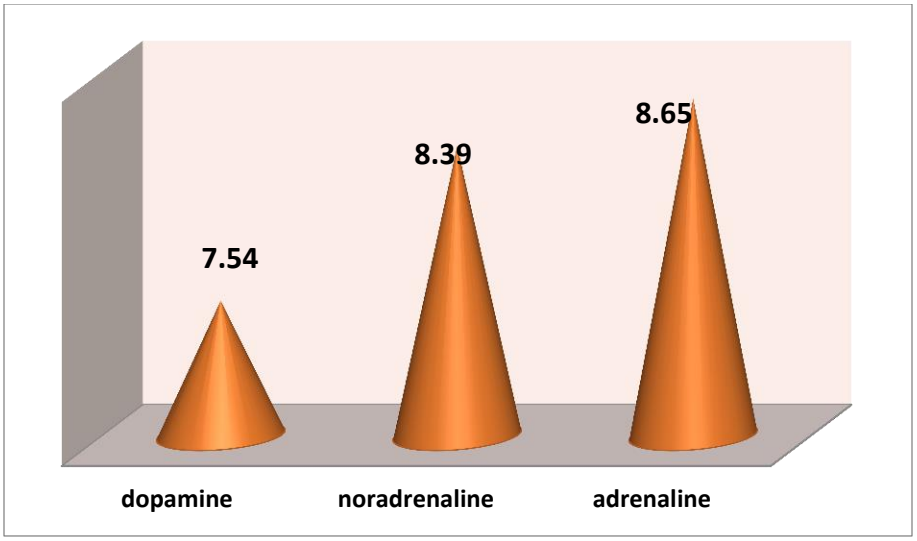

Figure 3 Central venous pressure (CVP) in the three study groups.

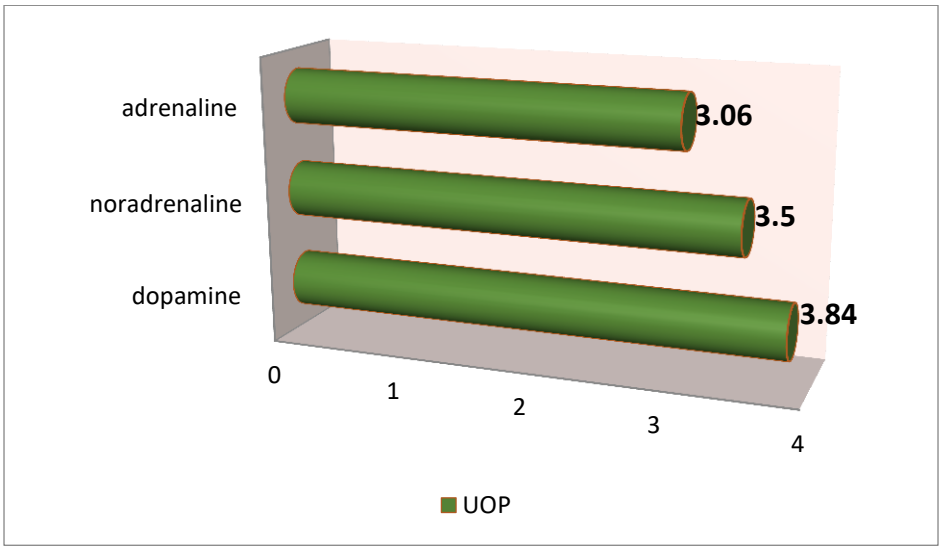

Figure 4 Urine output (UOP) in the three study groups.

As regards the blood gas (ABG) there was a significant difference regarding the outcome between the two groups in pH, P_aO_2, P_aO_2/F_iO_2 (P/F) ratio and base excess as shown in (Table 3) and figure 5, 6, 7.

Table 3 A comparisons between the three studied groups regarding the ABG parameters and oxygen index.

ABG Parameters	Dopamine group (n=20)	Noradrenaline group (n = 20)(%)	Adrenaline group (n =20)(%)	P-value	Sig
pH Mean (confidence interval)	7.30 (7.28-7.32)	7.32 (7.30-7.33)	7.28 (7.26-7.30)	0.031*	S*
P_aO_2 Mean (confidence interval)	98.84 (95.96-101.72)	97.51 (94.82 -100.20)	93.80 (91.05-96.54)	0.04*	S*
P_aO_2/F_iO_2Ratio Mean (confidence interval)	206.23 (189.51-222.95)	210.16 (194.53-225.79)	174.21 (158.29-190.13)	0.003*	S*
Base Excess Mean (confidence interval)	-1.56 (-2.82- -0.314)	-3.03 (-4.26 - -1.80)	-6.88 (-8.20 - -5.57)	0.000**	S*

ABG: Arterial blood gas, *pH:* Potential hydrogen, *P_aO_2:* Partial pressure of oxygen in arterial blood (mmHg), *PaCo2:* Partial pressure of carbon dioxide in arterial blood (mmHg), *P/F:* P_aO_2/F_iO_2.

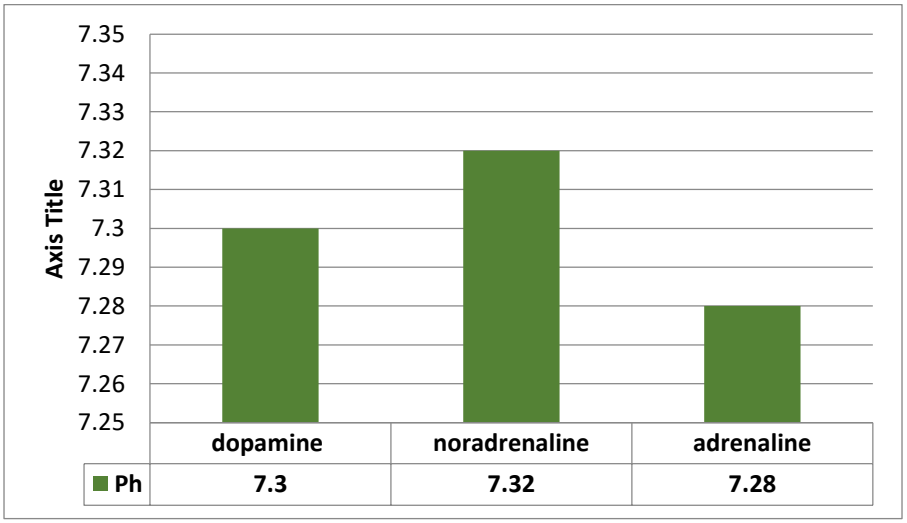

Figure 5 pH in the three study groups

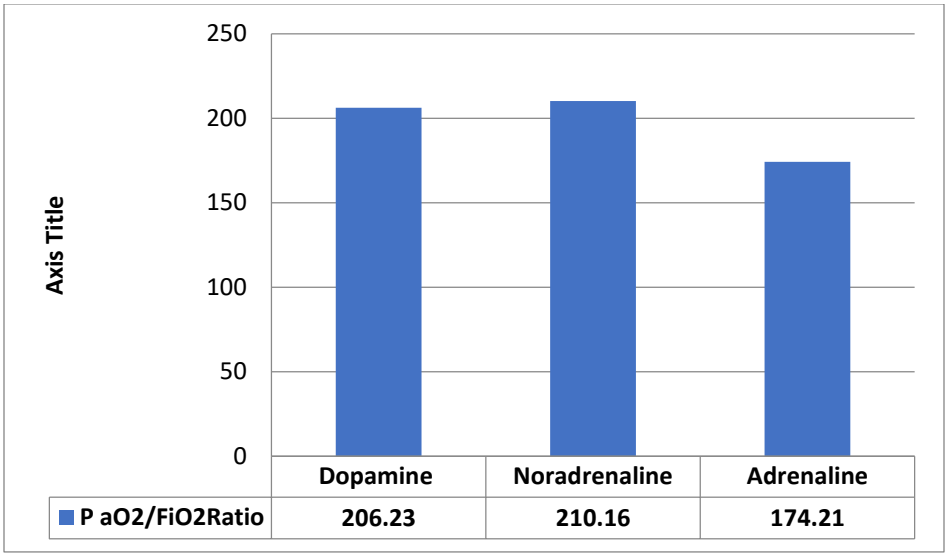

Figure 6 P_aO_2/F_iO_2 Ratio in the three study groups.

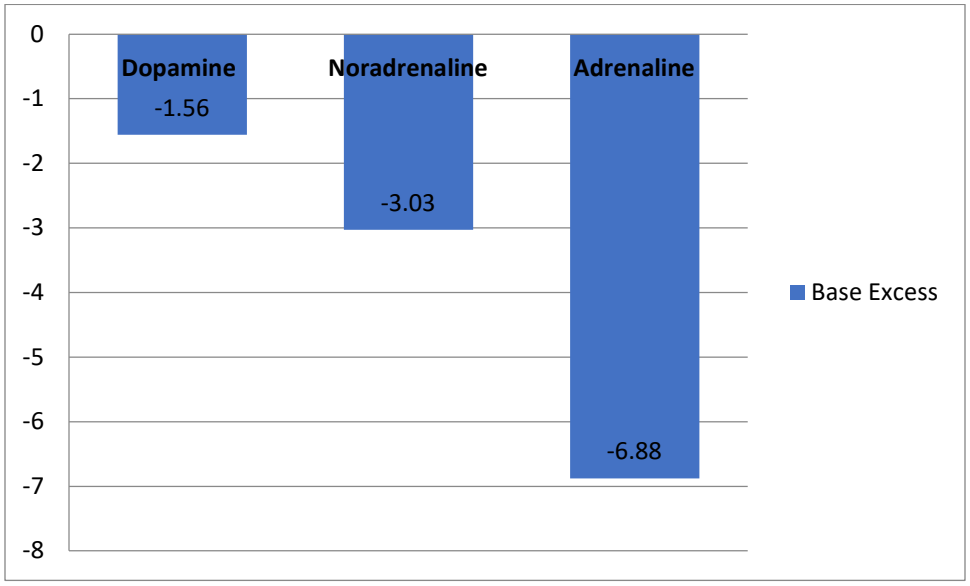

Figure 7 Base Excess in the three study groups.

As regards the echocardiography parameters there was a significant difference regarding the outcome between the three groups in SV, EF and FS as shown in (Table 4) and (figure 8, 9, 10).

Table 4 A comparison between the echocardiography parameters between three groups.

Eccho Parameters	Dopamine group (n=20)	Noradrenaline group (n = 20)(%)	Adrenaline group (n =20)(%)	P-value	Sig
SV Mean (confidence interval)	10.17 (8.93 – 11.41)	9.46 (8.31 – 10.67)	11.54 (10.38 – 12.70)	0.041*	S*
EF Mean (confidence interval)	54.81 (53.24 -56.37)	51.92 (50.46-53.39)	54.99 (53.54 -57.37)	0.021*	S*
FS Mean (confidence interval)	27.04 (26.19-27.90)	25.28 (24.46 -26.09)	27.25 (26.39-28.12)	0.01*	S*
LVOT VTI Mean (confidence interval)	14.58 (14.04 - 15.21)	14.87 (14.36 - 15.37)	14.91 (14.40 - 15.42)	0.675	NS
CI Mean (confidence interval)	2.83 (2.72 - 2.94)	2.64 (2.54 - 2.75)	2.79 (2.65 - 2.86)	0.058	NS

SV: stroke volume (mml), *EF:* ejection fraction (%), *FS:* fractional shortening (%), *LVOT VTI:* Left Ventricular Outflow Tract Time Velocity Index, CI: Cardiac Index.

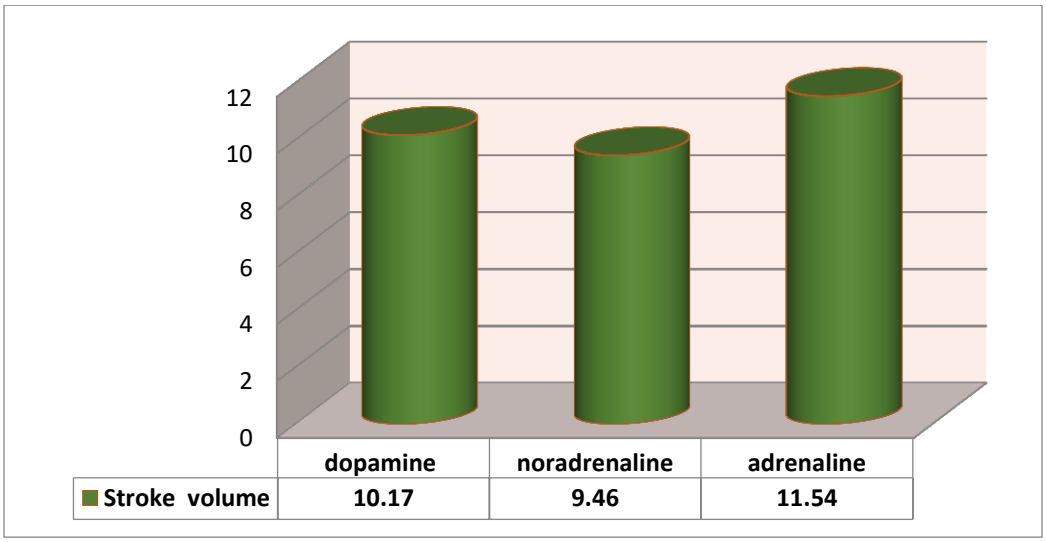

Figure 8 Stroke volume in the three study groups.

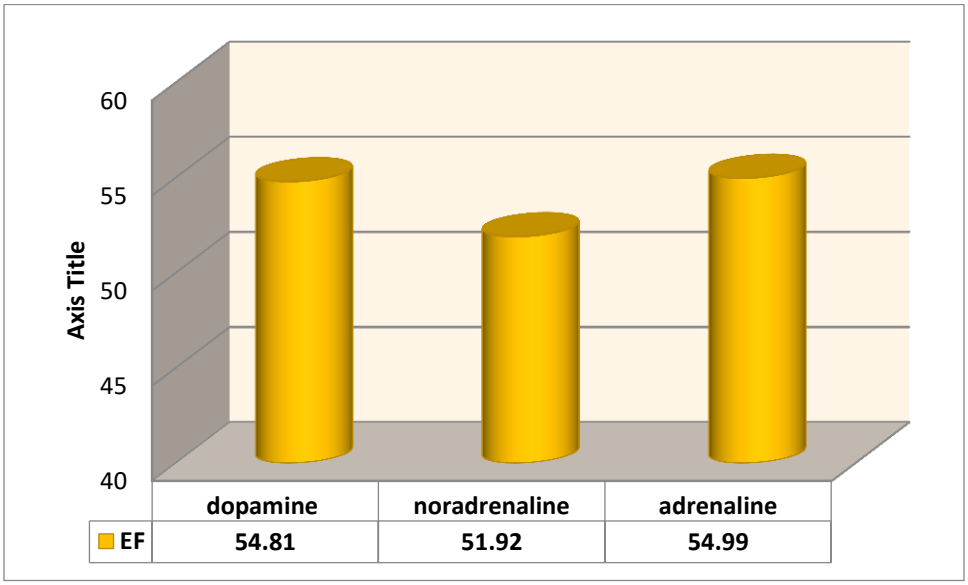

Figure 9 Ejection fraction (EF) in the three study groups.

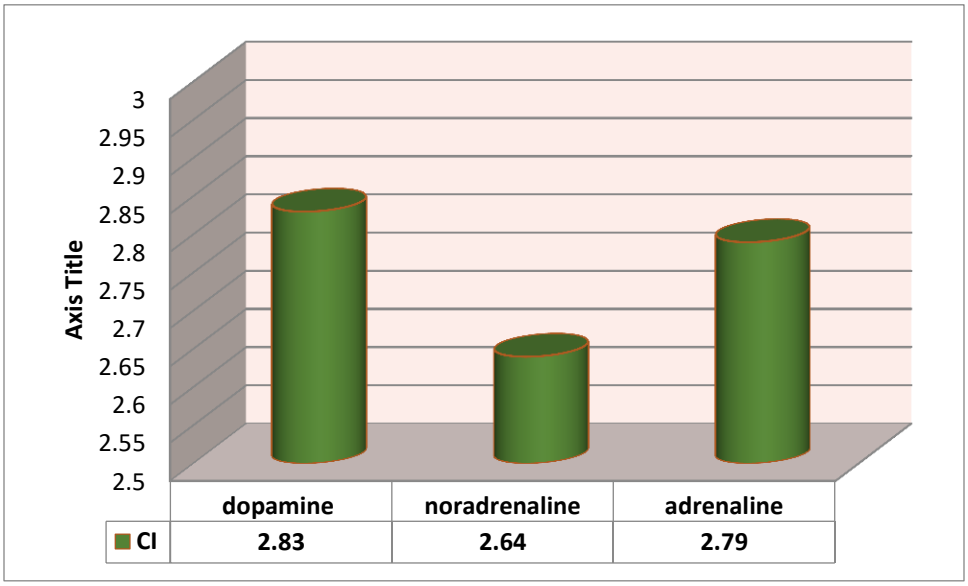

Figure 10 Cardiac Index (CI) in the three study groups.

4. DISCUSSION

In our study, we sought to monitor hemodynamic in septic shock patients in pediatric age group and to compare the effects of dopamine, nor-epinephrine and epinephrine on cardiac hemodynamic. Prospective observational study included 60 patients with septic shock presented to Pediatric Intensive Care Unit, Children's hospital, Ain Shams University who were enrolled after consideration of inclusion and exlusion criteria. They were evaluated before starting vasoactive drug and after twenty four hours. In our study male to female ratio was 1:1 with median age ranging in three groups between 11- 27 months.

In our study mechanical ventilation was needed in 48 patients (80%). In agreement with our study Razzaque et al., (2020), reported that mechanical ventilation was recorded in 75(75%) in his prospective study to evaluate 100 patients suffering from septic shock with mean age the as 2.16±3.26 years. Concerning the mean readings of vital data obtained before and after twenty four hours of initiating vasoactive medication, our analysis showed that mean blood pressure values were significantly higher in patients in noradrenaline group compared to other groups (P-value < 0.000). This is consistent with Baske et al., (2018) which stated that septic shock patients who received noradrenaline had mean blood pressure higher than who received adrenaline.

On the other hand Ventura et al., (2015) recorded higher mean blood pressure in 120 children septic patients, who received adrenaline compared to others who received dopamine. This variation may be due to the variable nature and severity of the major disease and various ages of the sample population. Regarding ABG data were recorded before and after twenty four hours of starting inotropic medications, our study showed significantly lower pH, PaO2 and lower P/F ratio in the adrenaline group in comparison to noradrenaline and dopamine groups. This is consistent with Backer et al., (2010) who reported a high statistically significant difference between the studied groups regarding P_aO_2 & P/F ratio. Also, Labib et al., (2016) found that ABG parameters including P_aO_2, P_aO_2/F_iO_2 were significantly lower in septic patients who received adrenaline than those who received dopamine or terlipressin. Several studies had used other indices of oxygen supply and delivery in patients with septic shock and comparing their levels before and after treatment. Agrawal et al., (2011) who reported that patients who received dopamine showed a significantly higher increase in post-treatment index of oxygen delivery compared to patients who received adrenaline.

In our study, there was a statistically significant difference between the echocardiography paramaters that were recorded before and after twenty four hours of starting inotropic medications, in the form of higher EF, FS, SV in the adrenaline group in comparison to noradrenaline and dopamine groups. In agreement with our study, Mahmoud & Ammar (2012) showed left ventricular ejection fraction was significantly higher in group who received adrenaline at the end of the study.

Several studies get to the conclusion of ejection fraction and fractional shortening improved after receiving fluid and different inotroping management. One of these studies, Knoester et al., (2008) who found that ejection fraction and shortening fraction improved after adrenaline infusion. But this study has some limitations as heterogenicity of the population both for indications and age and samples size is small. Larger studies which include all ages are recommended.

5. CONCLUSION

The use of echocardiography can help to choose and escalate vasoactive drug in patients with septic shock. Adrenaline is more effective than noradrenaline and dopamine in improving cardiac function. However noradrenaline is more potent on blood pressure.

Ethical approval: Approval of Faculty of Medicine Ain Shams University Research Ethics Committee (FMASU REC, FWA 000017585) was obtained for this study.

Informed consent

Written and oral informed consent was obtained from all individual caregivers included in the study.

Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

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Competing interests: The authors declare that they have no conflicts interests.

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Authors' contributions
EBA was a major contributor in data collection in addition to writing the manuscript, MSM was the main contributor in the study design and in data analysis, NMW revised the data set and participated in statistical analysis, ATA revised the data set and participated in data analysis. All authors read and approved the final manuscript.

Abbreviations
HR: Heart rate
MAP: Mean arterial blood pressure
CVP: Central venous pressure
EF: Ejection fraction
FS: fractional shortening
SV: Stroke Volume
PICUs: Pediatric Intensive Care Units.
FiO2: Fraction of inspired oxygen.
RR: Respiratory Rate.
PaO2: Partial pressure of oxygen (mmHg).
PaO2 / FiO2: Partial pressure of oxygen/ fraction of inspired oxygen.

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